REMARKS

In the Office Action dated June 28, 2007, claims 11-26, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 11-14, 16-21, 23, and 25-26 remain in this application, and claims 1-10, 15, 22 and 24 have been canceled.

An initial sequence listing is attached to this paper and its entry into the application is respectfully requested. The specification and claims have been amended to add sequence identifiers. No new matter is introduced by means of these amendments.

The specification was objected to due to commas where periods should be used. The specification has been amended to correct these informalities. In view of these amendments, applicants request that this objection be withdrawn.

Claims 14 and 21 were objected to as including undefined abbreviations. Claims 14 and 21 have been amended to correct these informalities. The description of MG132 can be found on page 3 of the present application. In view of these amendments, applicants request that these objections be withdrawn.

Claims 11, and 14-26 were rejected under 35 USC §112, second paragraph, as indefinite. The language "foreign matters" has been deleted from claim 11, claim 14 has been amended to clarify that the cardiac fibrosis is mediated by the rennin-angiotensin-system, and claim 21 has been amended to clarify that the organic compound has a relative molar mass ≤ 1000. The

amendments to claim 14 are supported by the disclosure on page 1, lines 20-27 and the amendments to claim 21 are supported by the disclosure on page 2, lines 19-21 of the present application.

Claims 21, 23, 25 and 26 were rejected under 35 USC §112, first paragraph as lacking an adequate written description. Claim 21 has been amended to clarify that modified peptide inhibitor is selected from the group consisting of a peptide boronate and a peptide aldehyde. Claim 23 has been amended to delete "a gene expression inhibitor of the proteasomal system" and to indicate that the binding protein or binding peptide is directed against ubiquitin and/or against the proteasome. Claim 25 has been amended to delete the term "derivative". Applicants respectfully point out that it is routine in the art to make antibodies or antigen binding parts when the targets are known. Claim 26 has been amended to delete the language "a double-stranded RNA (dsRNA)" and "a triplex forming oligonucleotide against a proteasome encoding sequence". Applicants respectfully point out that antisense and knock out technology was known in the art at the time the present invention was made and given the proteosome encoding sequences, one skilled in the art would be able to prepare antisense RNA and knock out constructs using the disclosure in the present application. In view of the above amendments, applicants request that this rejection be withdrawn.

Claims 11, 18-19 and 21-26 were rejected under 35 USC §102(e) as anticipated by Schubert. Schubert discloses agents for the treatment of viral infections. Schubert indicates that his invention can prevent, reduce or reverse

the consequences of a HBV and HCV infection, including liver cirrhosis/fibrosis. Applicants respectfully contend that liver cirrhosis/fibrosis which is caused by a viral infection is due to an inflammatory response to foreign matter. The present claims are directed to a method for treating fibrotic diseases which are not caused by inflammatory responses. Applicants are unclear as to why the office action states that Schubert's liver fibrosis which occurs as a consequence of a viral infection is not an inflammatory response to foreign matter. If this rejection maintained, applicants request an explanation of why fibrosis caused by a viral infection is not an inflammatory response to foreign matter. As discussed in the present application, the presently claimed invention treats fibrosis which is not due to an inflammatory response, such fibrosis can occur for example, as a result of overload of the myocardium, which may be caused by high blood pressure, myocardial infarction, or cardiomyopathies. Since Schubert's viruses would clearly cause an inflammatory response, applicants contend that Schubert does not anticipate the presently claimed invention and request that this rejection be withdrawn.

Claims 11-14, and 18-20 were rejected under 35 USC § 102(e) as anticipated by Pluenneke. Pluenneke discloses the administration of a TNF inhibitor in combination with a proteasome inhibitor. Pluenneke states that the proteasome inhibitor can induce apoptosis and thus can sensitize cancer cells to other anti-cancer agents. Applicant's note that claims 15-17 were not included in this rejection as the TNF inhibitor is clearly the main active ingredient in Pluenneke and thus Pluenneke does not disclose the proteasome inhibitor

dosages recited in claims 15-17. In order to advance the prosecution of the present application, claim 11 has been amended to recite the dosages recited in claim 15 and claim 15 has been canceled. In view of these amendments, applicants request that this rejection be withdrawn.

Claims 15-17 were rejected under 35 USC §103(a) as unpatentable over Pluenneke, As discussed above, claim 15 has been canceled and claim 11 has been amended to include the dosages recited in claim 15. Applicants contend that one would not be motivated to optimize the proteasome inhibitor used in Pluenneke's method for the treatment of fibrotic diseases because the TNF inhibitor is the main active ingredient in Pluenneke's treatment. The only description of a proteasome inhibitor in Pluenneke is in paragraph [0056] which discusses cancer treatments. This paragraph indicates that the proteasome inhibitor can sensitize cancer cells to other anticancer agents. Since Plueneke only indicates that the TNF inhibitor in combination with cytokine IFNγ-1b is useful for treating organ fibrosis, one skilled in the art would not try to optimize the dosage of the proteasome inhibitor for treating fibrotic diseases as in the present invention. In other words, Plueneke discloses a combination with TNF inhibitor is the main active ingredient. One skilled in the art would not try to optimize the combination treatment by trying different dosages of a minor ingredient and possibly deleting the main active ingredient. Applicants respectfully point out that Plueneke does not suggest or disclose that the proteasome inhibitor is useful for treating organ fibrosis, Plueneke only indicates that the proteasome inhibitor can sensitize cancer cells. Therefore, one skilled in

the art would not be motivated to optimize the dosage of the proteasome inhibitor for the treatment of fibrotic diseases. In view of the above discussion, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 11-14, 16-21, 23, and 25-26 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By 

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